Cancer-associated fibroblasts enhance the gland-forming capability of prostate cancer stem cells.

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Public Summary:
We present evidence that cancer-associated fibroblasts (CAFs) could enhance both the stemness and growth potentials of the cancer stem cells(CSCs). It is likely that these new clues could be further developed to better understand the biology of CSCs in prostate cancer and, potentially, in cancers in general.

Scientific Abstract:
Signals originating from cancer-associated fibroblasts (CAF) may positively regulate proliferation and tumorigenicity in prostate cancer. In this study, we investigated whether CAFs may regulate the biology of prostate cancer stem cells (CSC) by using a conditional Pten deletion mouse model of prostate adenocarcinoma to isolate both CAF cultures and CSC-enriched cell fractions from the tumors. CSCs that were isolated possessed self-renewal, spheroid-forming, and multipotential differentiation activities in tissue culture, segregating with a cell fraction exhibiting a signature expression phenotype, including SCA-1 (high), CD49f (high), CK5 (high), p63 (high), Survivin (high), RUNX2 (high), CD44 (low), CD133 (low), CK18 (low), and Androgen Receptor (low). CSC spheroid-forming efficiency was differentially influenced by the nature of fibroblasts in a coculture system: Compared with mouse urogenital sinus mesenchyme or normal prostate fibroblasts, CAFs enhanced spheroid formation, with the spheroids displaying generally larger sizes and more complex histology. Graft experiments showed that CSCs admixed with CAFs produced prostatic glandular structures with more numerous lesions, high proliferative index, and tumor-like histopathologies, compared with those formed in the presence of normal prostate fibroblasts. Together, our findings underscore a significant role of CAFs in CSC biology.